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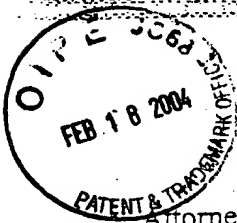
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Attorney Docket No. 9310.22CX

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

Application Serial No: 09/463,352

Group Art Unit: 1655

Filed: January 21, 2000

Examiner: B. Sisson

For: *NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN
THE AMPLICATION AND DETECTION OF ALL SUBTYPES OF HIV-1*

MAIL STOP RCE

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

DECLARATION OF JAAP GOUDSMIT,
PIETER OUDSHOORN, SUZANNE JURRIAANS
AND VLADIMIR VLADIMIROVICH LUKASHOV
UNDER 37 C.F.R. § 1.131

Sir:

We, Jaap Goudsmit, Pieter Oudshoorn, Suzanne Jurriaans and Vladimir Vladimirovich Lukashov hereby declare that:

1. We are the inventors of the subject matter of the rejected claims pending in the above-referenced patent application.
2. Prior to June 25, 1997, we conceived and reduced to practice the oligonucleotides having the nucleotide sequence of SEQ ID NOs 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11, respectively, as recited in the pending claims, as well as methods of use and kits employing these oligonucleotides to detect HIV-1 nucleic acid in a sample
3. In support of the above statement, we hereby submit as Appendix A a copy of relevant pages of an internal memorandum entitled "Feasability of a qualitative NASBA assay with a broad HIV-1 clade reactivity" prepared by non-inventor, F. Jacobs, under the direction of

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Jaap Goudsmit



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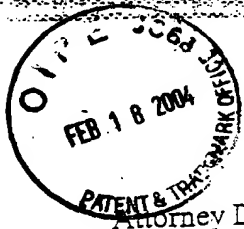
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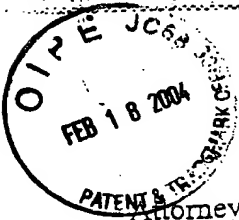
Suzanne J. Janssens

Date

Vladimir Vladimirovich Lukashov

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30 Oct 2003



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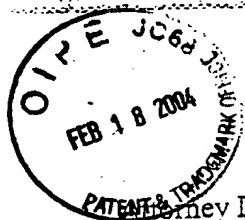
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Oktober 6, 2003



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Jaap Goudsmit
Jaap Goudsmit

October 3, 2003
Date

Pieter Oudshoorn

Date

Suzanne Jurriaans

Date

Vladimir Vladimirovich Lukashov

Date



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Pharma Group

Confidential

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Organon Teknika bv

R&D

Boxtel The Netherlands

Diagnostics

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Author:

Department	Name	Date	Signature
NDU	F. Jacobs		

Approval:

Function	Name	Date	Signature
Groupleader	P. Oudshoorn		

To be returned to R&D secretary before submitting for final approval

Final authorization:

Function	Name	Date	Signature
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2. Materials and methods

2.1 Design of primers and probes.

The oligonucleotide sequences are respectively:

P1.1: *aat tct aat acg act cac tat agg gAG AGG GGC GCC ACT GCT AGA GA*
P1.2: *aat tct aat acg act cac tat agg gAG AGG TTC GGG CGC CAC TGC TAG A*
U5 end: *aat tct aat acg act cac tat agg gCGGGCGCCACTGCTA*
P2.1: CTG CTT AAA GCC TCA ATA AA
P2.2: CTC AAT AAA GCT TGC CTT GA

To perform ECL detection one biotin probe and two different detection probes were designed with the following sequences:

HIV-1 LTR-bio: TCT GGT AAC TAG AGA TCC CTC
HIV-LTR-AMN1: TAG TGT GTG CCC GTC TGT.
HIV-LTR-AMN2: AGT GTG TGC CCG TCT GTT.

2.2 Evaluation and optimization of the primers and probes.

The primers were tested directly in the amplification in the combinations P1.1/P2.1, P1.1/P2.2, P1.2/P2.1, P1.2/P2.2 and U5-end/P2.2 on in vitro *LTR* RNA and on Scott Layne RNA (subtype B, stock solution of 5.5×10^9 copies RNA/ml). The input of the RNA was 10^4 copies. The amplifications were examined on a 2% agarose gel and then blotted in 1 hour on zeta probe and cross-linked with UV. The blot was hybridized with the biotin probe (3 μ M) by incubating the blot for 4 hours at 50°C. After hybridization the blot was washed two times for 5 minutes with 3*SSC/1%SDS solution at 50°C and one time for 10 minutes with 2*SSPE/0.1%SDS solution at RT. After this the blot was incubated for 30 minutes with 2 μ l streptavidine/HRP solution (500 U/ml, Enhanced ChemiLuminiscense detection kit from Amersham) in 10 ml 5*SSPE/0.5%SDS. The blot was again washed two times for 5 minutes in 2*SSPE/0.1%SDS solution and one time for 10 minutes in 2*SSPE solution. The blot was dried between tissues and developed with the development solutions from the enhanced chemiluminiscense kit (Amersham). The blot was wrapped in Saran wrap and a film was placed on the blot for a couple of seconds. The film was developed according to the standard procedures.

3.2 Evaluation of selected primers.

Figure 3. Detection of the amplimers on blot.

The primersets used were: nr 1: P1.1-P2.1, nr 2: P1.1-P2.2, nr 3: P1.2-P2.1, nr 4: P1.2-P2.2, nr 5: U5 end-5'LTRSph1. The RNA used as input were: A: in vitro RNA 10^4 copies per input, B: Scott Layne RNA 10^4 copies per input, C: No Templates.

